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Bleeding in a Patient With Lupus Anticoagulant Without Associated Hemostatic Abnormalities

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Bleeding is very rare in patients with lupus anticoagulants in the absence of associated hemostatic abnormalities. Few cases have been reported with attention given to work-up for other coagulation defects. We report a case of spontaneous hematoma in a patient with lupus anticoagulant, immunoglobulin (Ig)M anticardiolipin antibodies, and no other associated abnormalities. Am. J. Hematol. 59:258–259, 1998. © 1998 Wiley-Liss, Inc.

Key words: bleeding; lupus anticoagulant; associated hemostatic abnormalities

INTRODUCTION

The lupus anticoagulant (LA) is an antibody, either immunoglobulin (Ig)M, IgG, or both, that cross-reacts with an anionic phospholipid and beta 2-glycoprotein I, and is usually recognized by a prolonged activated partial prothrombin time (aPTT). The presence of LA is associated with arterial or venous thrombosis, recurrent fetal loss, or thrombocytopenia. A small subset of patients with LA may also have a deficiency of plasma prothrombin (factor II) and these patients may present with severe bleeding if the factor II level is below 20% of normal [1]. Other causes of bleeding in patients with LA, especially lupus patients, include thrombocytopenia, uremia, and anticoagulation. Although not necessarily associated with LA, antibodies to factor VIII, and very rarely, antibodies to fibrinogen, factor XIII, or von Willebrand factor are also potential causes of bleeding [2]. We report a patient with LA without associated hemostatic abnormalities who presented with spontaneous bleeding.

CASE REPORT

A 78-year-old patient with a history of coronary artery bypass graft and prostatic hypertrophy presented with pain in his left thigh of two days duration. He denied a history of trauma and was not taking anticoagulant or antiplatelet medication. He had no personal or family history of a bleeding disorder. Physical examination revealed a large hematoma in his left thigh which was confirmed by computed topography (CT) scan (Fig. 1). His hemoglobin, which had been 14.7 gm/dl four weeks earlier, was 12.6 gm/dl on admission. Additional laboratory data revealed a white blood cell (WBC) count of 6.8 $\times 10^9$/l, platelets of 201 $\times 10^9$/l, and normal chemistries. Coagulation studies revealed a normal prothrombin time (PT) of 12.4 sec (control, 11.9 sec), and an aPTT of 54.6 sec (control, 30.5 sec) that did not correct to the normal range after a 50:50 mix with normal plasma. The aPTT showed correction with the platelet neutralization procedure. A dilute Russell's Viper Venom test with the confirmatory test (American Diagnostic, CT) also detected the presence of LA. The thrombin time, fibrinogen level, bleeding time, and platelet aggregation assays, including ristocetin cofactor assay, were normal. Factor assays were: factor VIII, 15.4%; factor IX, 5.9%; and factor XI, 6.9%, with a prothrombin level of 62.1%. When the plasma was diluted 1:20 and 1:40 in buffer the apparent factor VIII levels increased to 24.2% and 48%, respectively (factor IX and XI levels also increased with dilution of the plasma). The IgM anticardiolipin antibody was 13,360 MPL/ml (normal, <10 MPL/ml), IgG <10 GPL/ml (normal, <10 GPL/ml), and IgA of 46 SDU (normal, <10 SDU). Serum protein electrophoresis showed a small monoclonal protein in the mid-gamma region that

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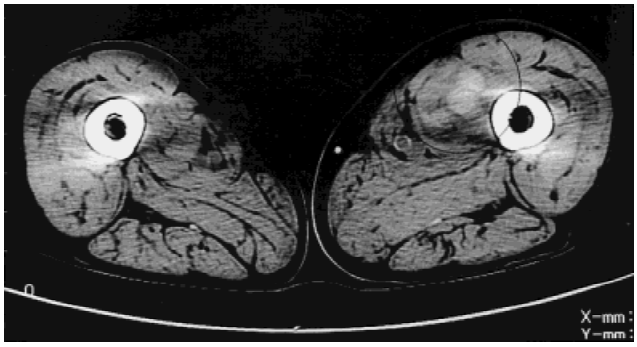

Fig. 1. CAT scan of the thighs in a patient with swelling and pain of his left thigh. The circle shows the hematoma.

was IgM kappa by immunoelectrophoresis, with normal polyclonal globulins. The patient was managed without specific treatment and, at follow-up after two years, he has had no further bleeding event although his aPTT remains elevated.

DISCUSSION

Bleeding is a very rare manifestation of the LA in the absence of associated factor II deficiency, thrombocytopenia, or vascular defect. In a study of 219 patients with LA at the Mayo Clinic there were only 17 episodes of bleeding [3]. Of these, 16 had associated anticoagulation, thrombocytopenia, or uremia. The one patient with no associated hemostatic defect had a prolonged PT in addition to a prolonged aPTT suggesting an associated hypoprothrombinemia, although this was not stated. Similarly, in another review of 35 patients with LA, five patients presented with spontaneous bleeding episode. Four of the patients had severe thrombocytopenia and one patient had no associated hemostatic defect, although more detail was not given [4]. There are two reported cases of patients with abnormal postoperative bleeding in which bleeding was attributed to the LA itself. In one of these, life-threatening bleeding occurred after abdominal surgery and a complete hemostatic profile was otherwise normal [5]. The bleeding responded rapidly to plasma exchange. In the other case, excessive bleeding occurred after a tooth extraction even though the patient received two units of fresh plasma preoperatively [6]. Three years later the patient was admitted for a strangulated inguinal hernia; he was given prednisone preoperatively which suppressed the LA and no excess bleeding occurred. A complete hemostatic profile was normal at that time.

Our patient had a spontaneous bleeding episode that resolved without any treatment and no further bleeding events have occurred despite the presence of a persistently elevated aPTT. There was no prothrombin deficiency, thrombocytopenia, uremia, acquired von Willebrand disease, detectable platelet defect, or abnormality of fibrinogen. Factor VIII, IX, and XI levels were low, consistent with an LA interfering with these assays. The apparent factor VIII level increased substantially with dilution of the patient plasma, ruling out a concomitant factor VIII inhibitor. We did not assay for an inhibitor of factor XIII. These rare inhibitors usually cause severe, potentially fatal bleeding [2].

Our case and that reported by Monoharan and Gottlieb [5] were both unusual or unexpected types of bleeding in patients with LA without associated hemostatic abnormalities. Interestingly, in both cases there was no subsequent bleeding on follow-up despite the persistence of the LA, raising the possibility of a transient, yet undefined associated defect. We suggest that subsequent reports of unusual bleeding in patients with LA include as complete and clearly defined hemostatic testing as possible to help better understand this entity.

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